

Washington State Health Care Authority

Denosumab Medical Policy

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Presentation Objectives

- To provide **background information** relevant to denosumab and its FDA-approved indications
- To present the proposed **medical policies** for **denosumab**

Background Information

Background Information

- Denosumab (marketed in the US as Prolia® and XGEVA®) is a monoclonal antibody which targets receptor activator nuclear factor kappa-B ligand (RANKL)^{1,2}.
- RANKL is an essential protein for the formation, function and survival of osteoclasts¹.
- Inhibiting RANKL leads to decreased osteoclast activity, thereby decreasing bone resorption and improving bone health¹.
- RANKL is a mediator of bone pathology in solid tumors with osseous metastases².
- RANKL is expressed on stromal cells in giant cell tumors of bone².

1.) Prolia® (denosumab) [prescribing information]. Thousand Oaks, CA: Amgen Inc; February 2015.

2.) Xgeva® (denosumab) [prescribing information]. Thousand Oaks, CA: Amgen Inc; June 2015.

Background Information

- Denosumab (both Prolia® and XGEVA®) is FDA-approved for use in many medical conditions:
 - Treatment of osteoporosis in postmenopausal women¹
 - Treatment to increase bone mass in men with osteoporosis¹
 - Treatment to increase bone mass in breast cancer with aromatase inhibitor (AI) therapy¹
 - Treatment to increase bone mass in prostate cancer with androgen deprivation therapy (ADT)¹
 - Prevention of skeletal-related events in bone metastasis from solid tumors²
 - Treatment of giant cell tumor of bone (GCTB)²
 - Treatment of hypercalcemia of malignancy refractory to bisphosphonates²
- Likewise, denosumab is not approved for many related or similar medical conditions^{1,2}:
 - Prevention of osteoporosis
 - Prevention or treatment of glucocorticoid-induced osteoporosis
 - Prevention of skeletal-related events in multiple myeloma

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2.) Xgeva® (denosumab) [prescribing information]. Thousand Oaks, CA: Amgen Inc; June 2015.

Background Information

- National guidelines for osteoporosis favor initiating pharmacotherapy for anyone with T-scores of -2.5 or lower at femoral neck, total hip, or lumbar spine.
 - Guidelines differ in their recommendations as first-line:
 - The American Association of Clinical Endocrinologists (AACE) recommends alendronate, risedronate, zoledronic acid, and denosumab.
 - The National Osteoporosis Foundation (NOF) recommends FDA-approved pharmacotherapy.
 - The National Guidelines Clearinghouse (NGC) recommends bisphosphonates.
- National guidelines for breast cancer recommend initiating pharmacotherapy for patients on aromatase inhibitors
 - Guidelines generally recommend bisphosphonates as initial therapy but may also consider denosumab
- National guidelines for prostate cancer recommend initiating pharmacotherapy for patients on androgen deprivation therapy
 - Guidelines recommend bisphosphonates (alendronate, zoledronic acid) and denosumab, although NGC specifically mentions zoledronic acid

Background Information

- National guidelines on metastatic cancer to the bone recommend using supportive therapy to prevent skeletal-related events (SREs)
 - Guidelines generally recommend IV bisphosphonates and denosumab, although oral ibandronate has been studied in this setting with positive results
- National guidelines on giant cell tumor of bone that is unresectable or is resectable with unacceptable morbidity recommend to be treated with denosumab, chemotherapy with interferon, or radiation therapy
 - Bisphosphonates have been studied in this disease state and was used prior to approval of denosumab
- National guidelines on hypercalcemia of malignancy generally recommend IV bisphosphonates, particularly zoledronic acid
 - Denosumab is recommended for patients refractory to bisphosphonates

Medical Policy

Medical Policy: Prolia®

Prolia® may be considered medically necessary for the treatment of FDA-approved indications when the patient meets **ALL** of the following criteria:

INCLUSION CRITERIA

1. Patient meets at least one of the following:

- a. patient is a man or postmenopausal woman and is diagnosed with osteoporosis, defined as a T-score of -2.5 or lower at the femoral neck, total hip, or lumbar spine; **OR**
- b. a. patient is a man who is receiving androgen deprivation therapy (ADT) for non-metastatic prostate cancer; **OR**
- c. patient is a woman who is receiving adjuvant aromatase inhibitor (AI) therapy for breast cancer; **OR**
- d. history of osteoporotic fracture; **OR**
- e. multiple risk factors for fracture, defined as WHO FRAX 10-year probability of a hip fracture $\geq 3\%$ or a 10-year probability of a major osteoporosis-related fracture $\geq 20\%$ based on US-adapted WHO algorithm; **AND**

Medical Policy: Prolia®

2. Patient has tried and failed (failure defined as an intercurrent fracture following one year of treatment or a significant decrease in bone density while on treatment after ruling out other causes, such as adherence, malabsorption, or calcium or vitamin D deficiencies), is intolerant to, or has a contraindication to:
 - a. at least one oral bisphosphonate; **AND**
 - b. intravenous zoledronic acid

EXCLUSION CRITERIA

1. Denosumab is prescribed for the prevention or the treatment of glucocorticoid-induced osteoporosis¹.
2. Patient has ANY of the following contraindications¹:
 - a. Uncorrected pre-existing hypocalcemia
 - b. Patient is pregnant
 - c. Patient is currently receiving XGEVA® (denosumab)

Medical Policy: XGEVA®

XGEVA® may be considered medically necessary for the treatment of FDA-approved indications when the patient meets **ANY** of the following criteria:

INCLUSION CRITERIA

1. Patient has bone metastases from solid tumors **AND** patient has tried, is intolerant to, or has a contraindication to intravenous zoledronic acid; **OR**
2. Patient is an adult or skeletally mature adolescent with giant cell tumor of bone that is unresectable or where surgical resection is likely to result in severe morbidity; **OR**
3. Patient has hypercalcemia of malignancy, defined as albumin-corrected calcium of >12.5 mg/dL due to malignancy after ruling out other causes, **AND** patient has tried and failed (failure defined as refractory hypercalcemia after at least 7 but no more than 30 days of IV bisphosphonate therapy per episode of hypercalcemia), is intolerant to, or has a contraindication to intravenous zoledronic acid or intravenous pamidronate

Medical Policy: XGEVA®

EXCLUSION CRITERIA

1. Denosumab is being prescribed for the prevention of skeletal-related events in patients with multiple myeloma, for the prevention of all osteoporosis, or for the treatment of glucocorticoid-induced osteoporosis².
2. Patient has ANY of the following contraindications^{1,2}:
 - a. Uncorrected pre-existing hypocalcemia
 - b. Patient is pregnant
 - c. Patient is currently receiving Prolia® (denosumab)

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Questions?

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Works Cited

- 1.) Prolia® (denosumab) [prescribing information]. Thousand Oaks, CA: Amgen Inc; February 2015.
- 2.) Xgeva® (denosumab) [prescribing information]. Thousand Oaks, CA: Amgen Inc; June 2015.